REMARKS/ARGUMENTS

With this amendment, claims 1, 6, 14-16, 19, 28, and 29 are pending. Claims 2-5, 7-13, 17, 18, and 20-27 have been cancelled. Claim 1 has been amended and new claims 28 and 29 have been added. For convenience, the Examiner's rejections are addressed in the order presented in the August 12, 2003 Office Action.

I. Status of the claims

Claim 1 has been amended to delete the hybridization conditions and to recite an ILKAP polypeptide that has "at least 90% identity to an amino acid sequence of SEQ ID NO:2." This amendment adds no new matter. Support for this amendment can be found in the specification, e.g., on page 4, lines 22-24.

Claim 1 has been amended to recite "angiogenic or loss of angiogenesis phenotypic effect." This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 26, line 16.

Claim 28 has been added to recite an ILKAP polypeptide that has "at least 95% identity to an amino acid sequence of SEQ ID NO:2." This claim adds no new matter. Support for this amendment can be found in the specification, e.g., on page 4, lines 22-24.

Claim 29 has been added to recite assays for determining angiogenic or loss of angiogenesis phenotype. This claim adds no new matter. Support for this amendment can be found, e.g., in the specification on page 5, lines 30 and 33-34.

II. Rejection under 35 U.S.C. §112, first paragraph, enablement

1. Introduction

Claims 1-6, 14-16, and 19 were rejected as allegedly claiming subject matter that is not enabled by the specification. The Office Action states that nucleic acids encoding polypeptide variants are not enabled, as "the instant claims encompass in their breadth any ILCAP [sic] polypeptide encoded by a nucleic acid that hybridizes under stringent conditions to a complement of a nucleic acid encoding a polypeptide comprising an amino acid sequence of

SEQ ID NO:2." Office Action, page 3, lines 3-5. The Examiner further states that "one skilled in the art cannot use any functional effect as indicators of a test to determine a compound's anti-angiogenic potential." Office Action, page 3, line 12-13.

As identified in the Patent Office and the Federal Circuit, whether undue experimentation is required by one skilled in the art to practice an invention is determined by considering factors such as the amount of guidance presented in the application, the state of the prior art, and the presence of working examples. *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985); *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). As described in *Wands*, a "considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should precede." *Wands*, 8 USPQ2d at 1404 (quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982).

The claimed methods now specify that the ILKAP polypeptide has at least 90% identity to a reference amino acid sequence. Methods for determining percent identity are disclosed in the specification and are also well known to those of skill in molecular biology. These elements therefore provide adequate guidance for routine identification of the nucleic acids of the invention. In addition, claims now specify that the compound is identified by examining its angiogenic or anti-angiogenic effect on a cell expressing ILKAP. Therefore, modulation of the ILKAP polypeptide by the test compound is correlated by angiogenic or anti-angiogenic phenotype. Thus, undue experimentation is not required to practice the claimed invention.

2. The claimed reference sequences provide meaningful structural features that allow one of skill to practice the claimed invention without undue experimentation.

The rejection alleges that the specification provides enablement only for identification of compounds that modulate angiogenesis using a nucleic acid encoding an ILKAP polypeptide comprising an amino acid sequence of SEQ ID NO:2 or for a nucleic acid that hybridizes under stringent conditions to the full length of a nucleic acid that encodes SEQ ID NO:2. Furthermore, the rejection states that the only functional effect that correlates an anti-

angiogenic phenotype with the ILKAP polypeptide is an assay for avb3 integrin cell surface expression.

However, the claims now recite both functional and structural characteristics of the ILKAP nucleic acids of the invention. The present application also provides functional assays for identification of nucleic acids encoding ILKAP polypeptides of the invention, without undue experimentation. The assays and examples of the specification, together with standard methodology known to those of skill in the art, therefore provide adequate guidance for identifying claimed nucleic acids that encode the ILKAP polypeptides of the invention.

The assertion of undue experimentation appears to be based on an assumption that enablement requires the description of each and every nucleic acid that could be used in the claimed methods. As noted below, such a requirement is not consistent with the patent laws. Indeed, it is well settled in the biotechnology art that routine screening of even large numbers of samples is not undue experimentation when a probability of success exists. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Using the conditions set forth in the claims and specification and routine methodology, any competent laboratory technician in a molecular biology laboratory could isolate and prepare appropriate constructs, transform cells, and identify those nucleic acids that encode an ILKAP protein of the invention having at least 90% identity to SEQ ID NO:2. As set forth in MPEP § 2164.08, a rejection for undue breadth is inappropriate where "one of skill could readily determine any one of the claimed embodiments." In the present case, one of skill, given the specified 90% identity to reference sequence SEQ ID NO:2, could easily screen for other nucleic acid and protein molecules that can be used in the claimed methods.

The present invention describes a method of identifying compounds that modulate angiogenesis using a family of nucleic acids encoding polypeptides which functionally are ILKAP polypeptides involved in angiogenesis and which structurally encode a polypeptide having at least 90% identity to a reference ILKAP polypeptide.

At the time of the present invention, identification of nucleic acids having the functional and structural characteristics described above was well within the means of one of skill of the art, without undue experimentation. The present specification provides working examples and discloses standard techniques known to those of skill in the art, for the

identification of functional ILKAP polypeptides such as that exemplified by SEQ ID NO:2 (*see, e.g.*, specification at page 12, line 22 through page 13, line 17).

3. The claims require that the compound modulate the angiogenic characteristics of ILKAP

Moreover, functional assays to identify compounds modulating ILKAP polypeptides (*i.e.*, with angiogenic or anti-angiogenic phenotypes) of the invention are known to those of skill in the art and are disclosed in the specification. For example, the specification describes methods of determining an effect on angiogenesis through disclosure of multiple angiogenesis assays. Assays for angiogenesis include assays for expression of cell surface markers, such as $\alpha v\beta 3$ (page 3, page 5, page 17, and exemplified in Example 1 at pages 44-45); haptotaxis assays (page 3, page 5, page 17, and exemplified in Example 1 at page 45); a chick CAM assay (pages 5 and 29); a mouse corneal assay (pages 5 and 29); and assays for neovascularization of tumors (pages 6 and 29).

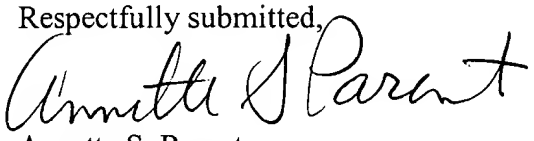
The assays described in the specification, coupled with methodology well known to those of skill in the art, therefore demonstrate that screening for compounds that modulate the angiogenic characteristics of an ILKAP polypeptide is routine. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Applicants therefore respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,



Annette S. Parent
Reg. No. 42,058

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
60119755 v1